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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,728	05/01/2002	Abraham J. Domb	PG 101	6100
23579	7590	05/24/2004	EXAMINER KRISHNAN, GANAPATHY	
PATREA L. PABST PABST PATENT GROUP LLP 400 COLONY SQUARE SUITE 1200 ATLANTA, GA 30361			ART UNIT 1623	PAPER NUMBER
DATE MAILED: 05/24/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/031,728

Applicant(s)

DOMB, ABRAHAM J.

Examiner

Ganapathy Krishnan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Specification

The disclosure is objected to because of the following informalities: At page 5 of the specification the citation WO 97/462 should be corrected to read WO 97/46223.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3, 5, 6, 10-13, 15-15-17 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites dextrans and alginates. It is not clear what applicant intends by these plurals. If these terms are meant to include derivatives then in the absence of the specific derivatizations to the chemical core claimed or distinct language to describe the structural modifications or the chemical names of the derivatives of this invention, the identity of said derivatives would be difficult to describe and the metes and bounds of the said derivatives applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in this and all other such recitations.

Claim 3 recites the types of bonds through which the saccharide units are connected. It is not clear what the recitation means since in polysaccharides the saccharide units are connected via ether linkages.

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Claim 6 recites $x+y+z+$. It is not clear if there is additional text intended after the + sign on the right of the z variable. If no additional text is intended then the + sign to the right of the z variable should be removed.

Claims 8, 10 and 17 recite the term derivatives. In the absence of the specific derivatizations to the chemical core claimed or distinct language to describe the structural modifications or the chemical names of the derivatives of this invention, the identity of said derivatives would be difficult to describe and the metes and bounds of the said derivatives applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated.

Claims 10 and 11 recite the term "oligomers". It is not clear if the term "oligomers" is intended to mean different sizes of the polymers. This plurality of polymers renders the claims indefinite.

Claim 15 recites, "predetermined type of cell or tissue". It is not clear what this means. For the purpose of prosecution it is interpreted to mean any type of cell.

Claim 19 recites cationic and/or non-ionic lipid and cationic and non-ionic polymers. It is not clear if both lipid and polymers are present as carriers or only one of them is present.

Claims that depend from base claims that are indefinite/unclear are also rendered indefinite/unclear.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

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Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of copending Application No. 10,044,538 ('538 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 2 and 3 of the copending '538 application are drawn to a composition comprising a polysaccharide chain having saccharide units ranging from 2 to 2000, at least one oligoamine having at least two amino groups grafted to the polysaccharide per each segment of 5 saccharide units and at least one further grafted group which is hydrophobic or amphiphilic grafted covalently to the polysaccharide chain per each segment of 50 saccharide units the group having at least 4 carbons and wherein the hydrophobic or the amphiphilic group is complexed with an anionic macromolecule selected from polynucleic acids, proteins and polysaccharides that are anionic and the said composition of claim 2 wherein the anionic molecules are selected from plasmid, open chain polynucleic acid, an oligonucleotide, an antisense, a peptide, a protein, a polysaccharide and combinations thereof. These recitations are seen in claim 1 of the instant application. The only additional recitation seen in claim 1 of the instant application is the molecular weight of 2000 daltons for the oligoamine.

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Claims 1 and 19 of the copending '538 application are drawn to a composition comprising a polysaccharide chain having saccharide units ranging from 2 to 2000, at least one oligoamine having at least two amino groups grafted to the polysaccharide per each segment of 5 saccharide units and at least one further grafted group which is hydrophobic or amphiphilic grafted covalently to the polysaccharide chain per each segment of 50 saccharide units the group having at least 4 carbons and the composition according to claim 1 (claim 19 is dependent on claim 1 or 2) in combination with cationic and nonionic lipids or polymers. Claims 1, 16 and 19 are drawn to the same polycation composition in association with an anionic macromolecule and also cationic and nonionic lipids and polymers. An overlap is seen between instant claims 1, 16 and 19 and claim 1 of the copending '538 application because of the recitation "cationic and nonionic lipids or polymers". Because of this and similar recitations in dependent claims, there is substantial overlap seen in claims 1-19 of the instant application with claims 1-24 of the copending '538 application.

It would have been obvious to one of ordinary skill in the art that the claims of the instant application and those of the copending application are substantially overlapping. The compositions of the instant invention must contain new and distinguishable limitations over the copending application to be patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1, 5, 7, 12-16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Jung et al (WO 93/25239).

Jung et al teach the preparation of a conjugate of arabinogalactan (polysaccharide with saccharide units in the range of 2 to 2000) and polylysine (oligoamine with two amino groups). The molecular weight of the polylysine is in the range of 1000-4000 daltons (polypeptide of upto 20 amino acids with at least 50% of the amino acids being lysine and having an amino branching). The conjugate showed the presence of an amine group (amine bond) (page 17, Example 6). The conjugate of Jung is seen to have at least one polylysine (oligoamine) attached (grafted) to the arabinogalactan chain per each segment of 5 saccharide units. Jung also teach a complex of the modified arabinogalactan with therapeutic agents, wherein the agents are polypeptides, a DNA molecule and an antisense molecule (page 9, lines 3-4; page 17, example 6, and page 29, line 30 through page 30, line 8). Jung's invention is also drawn to a method of delivery of therapeutic agents complexed to arabinogalactan into cytoplasm of cells (page 6, lines 9-13). This indicates that the complexes are not toxic or immunogenic. The polylysine in addition to the amino group also has a carboxylate group that can act as a ligand that facilitates binding of the said composition.

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These teachings of Jung et al are seen to meet the limitations of claims 1, 5, 7, 9, 12-16 and 18.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4, 6, 8, 9, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jung et al (WO 93/25239) in combination with RU 2027190 and Domb (US 6011008).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is drawn to a composition comprising a linear polysaccharide with at least one oligoamine having at least two amino groups and a molecular weight of upto 2000 daltons grafted to it. Dependent claims 2, 4, 6, 8, 9, 17 and 18 reciting limitations drawn to specific polysaccharides including synthetic polysaccharides, oligoamines with structures encompassed by a general formula, wherein the oligoamine is spermine or a derivative or ethyleneimine, and a pharmaceutical composition with a pharmaceutically acceptable carrier

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Jung et al teach the preparation of a conjugate of arabinogalactan (polysaccharide with saccharide units in the range of 2 to 2000) and polylysine (oligoamine with two amino groups). The molecular weight of the polylysine is in the range of 1000-4000 daltons (polypeptide of upto 20 amino acids with at least 50% of the amino acids being lysine and having an amino branching). The conjugate showed the presence of an amine group (amine bond) (page 17, Example 6). The conjugate of Jung is seen to have at least one polylysine (oligoamine) attached (grafted) to the arabinogalactan chain per each segment of 5 saccharide units. Jung also teach a complex of the modified arabinogalactan with therapeutic agents, wherein the agents are polypeptides, a DNA molecule and an antisense molecule (page 9, lines 3-4; page 17, example 6, and page 29, line 30 through page 30, line 8). Jung's invention is also drawn to a method of delivery of therapeutic agents complexed to arabinogalactan into cytoplasm of cells (page 6, lines 9-13). This indicates that the complexes are not toxic or immunogenic. The polylysine in addition to the amino group also has a carboxylate group that can act as a ligand that facilitates binding of the said composition.

Jung also teaches another embodiment wherein arabinogalactan can be used to create aldehyde groups. The aldehyde groups can be reacted with diamino compounds to form Schiff base followed by reduction with sodium borohydride. The resulting amino compound can be used to form a complex with therapeutic agents (page 9, lines 18-24).

However, Jung et al do not teach a composition wherein the polysaccharide is one selected from dextrans, pullulan, cellulose, cellobiose, inulin, chitosan, alginates and hyaluronic acid, wherein the polyamines are of the general formula as in claim 6 or spermine or ethyleneimine and a pharmaceutical composition.

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RU 2027190 teaches a conjugate of a polysaccharide and polyethyleneimine that has several advantages. But RU 2027190 does not teach a composition of the said conjugate with anionic macromolecules.

Domb et al teach conjugates of polysaccharides like dextran via reduction of a Schiff base to the corresponding conjugate with an amine bond. The polysaccharides could be natural or synthetic (see figure 1; col. 3, lines 14-31 and examples in col. 5 through col. 8).

Based on the teachings of Jung, RU 2027190 and Domb, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising a polysaccharide having at least one oligoamine in association with an anionic macromolecule with a reasonable amount of success since such compositions are taught by Jung and analogous conjugates are taught by RU 2017190 and Domb. Domb's teaching of the use of both arabinogalactan and dextran in his invention are representative of the other polysaccharides as instantly claimed. One of ordinary skill in the art also knows that water is a universally accepted pharmaceutical carrier and can be used to make pharmaceutical compositions.

One of ordinary skill in the art would be motivated to make a composition as instantly claimed since Jung teaches that charged macromolecules like nucleic acids can adhere or associate to conjugates of polysaccharides and polyamines via ionic bonding (page 9, lines 3-8). Hence the macromolecules complexed via ionic bonding can be released relatively easily unlike attachment via covalent bonding wherein a bond-breaking step like hydrolysis has to take place to release the agent.

Conclusion

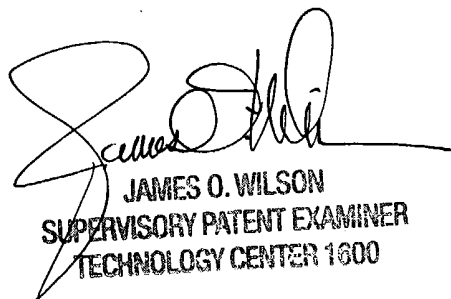
Claims 1-19 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK



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